the limit with that it is the second with specific with specific such that the second second specific such specific such second second

ANOVA of ADHD score for the genotypes of 20 genes

or in radional our property of the tracks.	200											
Gene	=			12			22			F-ratio	a	Gene score
	z	Mean	S	z	Mean	SS	z	Mean	SS			
Dopamine genes DRD1 SNP Ddel												
Lit Optmized	39	20.10	10.2	16	17.58	17	133	18.30	10.9	0.848	0.43	201 201
DRD2 SNP Tag IA												000
Optimized	15	15.93	10.3	120	19.50	10.2	201	17.51	11.4	1.560	0.21	021
LIG SNP MSCI	ç •	69		ţ	0		,	9	9 0	408	6	202
Optimized DRD4 * 48 bp repeat	152	28.	7.1	\c)	16.34	0.	17.	9.10	o O	0.480	50	70
Lit	99	19.00	10.9	162	17.98	10.5	118	17.86	11.6	0.223	0.80	200 200
<i>DRD5</i> 4 dinucleotide repeal Lit										;	:	220
Optimized	74	18.63	11.4	Ξ	19.15	11.3	151	17.38	10.6	0.881	0.41	120
Lit Lit Optimized	21	15.33	12.4	142	17.41	10.9	173	19.07	10.8	1.619	0.20	012 012
Serotonin genes												
HTT 4 (SLC6A4) promoter ins/del												000
Lit Optimized	85	16.20	10.9	159	19.11	10.9	9	18.28	11.3	1.953	0.14	021
HTB1A SNP C-1918G												022
Optimized	82	19.00	10.01	177	17.31	11.4	11	19.89	10.1	1.683	0.19	102
HIRIB (HIRIDB) SNP G861C Lt												005
Optimized	202	18.49	10.9	107	17.30	=	27	19.00	11.5	0 496	0.61	102
HTR1DA SNP T1350C Ind												02-
Optimized	266	18.16	113	20	19.34	9.7	ν,	,		0.641	0.43	02.
HTRZA SNP T102C Mspl		-										010
Ul Optimized	58	17.88	11.2	172	18.59	11.0	106	17.61	11.0	0.279	0.76	020
TDO2 SNP G. > A Int 6BsA												8
Lit Optimized	315	17.98	11.0	11	20.65	10.4	ν,			0.951	0.33	02-
<i>TPH</i> SNP A 779 C												600
Lit Optimized	99	19.00	10.4	180	17.73	10.8	96	19 28	11.5	0.705	0.495	202

Figure 1(a) (continued)

Mean SD N Mean SO N Mean SD N Mean SD N 18.81 10.1 168 18.78 11.1 101 16.69 11.3 17.42 11.1 128 18.8 10.5 22 21.95 11.7 11.8 18.14 11.5 158 18.46 10.6 23 19.73 9.6 0 17.82 11.2 144 19.04 10.6 38 16.6 11.3 0 16.89 11.1 156 19.59 10.9 66 17.58 10.9 2.	Gene	=			5			8					
Note the proof of the service of the		-			ي 			27			F-ratio	α,	Gene score
196 17.42 11.1 128 18.8 10.5 22 21.95 11.7 18 18.9 10.5 22 21.95 11.7 18 18.9 10.5 22 21.95 11.7 18 18.77 10.5 11.3 15.79 11.0 92 20.17 11.2 4 15.5 17.82 11.2 144 19.04 10.6 38 16.6 11.3 0 104. G1947A, Maill 16.89 11.1 156 19.59 10.9 66 17.58 10.9 2		z	Mean		z	Mean	SO	Z	Mean		ı		
67 18.81 10.1 16.8 18.78 11.1 101 16.69 11.3 186 17.42 11.1 128 18.8 10.5 22 21.95 11.7 155 18.14 11.5 158 18.46 10.6 23 19.73 9.6 (131 18.77 10.5 113 15.79 11.0 92 20.17 11.2 4 155 17.82 11.2 144 19.04 10.6 38 16.6 11.3 0 110 16.89 11.1 156 19.59 10.9 66 17.58 10.9 2	Norepinephine genes									- 1			
186 17.42 11.1 128 18.8 10.5 22 21.95 11.7 155 18.14 11.5 158 18.46 10.6 23 19.73 9.6 (1.3 18.77 10.5 11.3 15.79 11.0 92 20.17 11.2 4 155 17.82 11.2 144 19.04 10.6 38 16.6 11.3 0 110 16.89 11.1 156 19.59 10.9 66 17.58 10.9 2 25 18.45 10.8 10.9 2 25 18.45 10.8 10.9 2 25 18.45 10.8 10.9 2 25 18.45 10.8 10.9 2 25 18.45 10.8 10.9 2 25 18.45 10.8 10.9 2 25 18.45 10.8 10.9 2 25 18.45 10.8 10.8 10.9 2 25 18.45 10.8 10.8 10.9 2 25 18.45 10.8 10.8 10.9 2 25 18.45 10.8 10.8 10.8 10.8 10.8 10.8 10.8 10.8	UST 5/12 189 1												
186 17.42 11.1 128 18.8 10.5 22 21.95 11.7 155 18.14 11.5 158 18.46 10.6 23 19.73 9.6 131 18.77 10.5 113 15.79 11.0 92 20.17 11.2 155 17.82 11.2 144 19.04 10.6 38 16.6 11.3 110 16.89 11.1 156 19.59 10.9 66 17.58 10.9 75 19.42 10.8 17.5 16.5 17.5 10.9	Oplimized ADRA2A SNP promater region Mspl	29	18.81	10.1	168	18.78	11.1	101	16.69	11.3	1.285	0.28	220 220
155 18.14 11.5 158 18.46 10.6 23 19.73 9.6 131 18.77 10.5 113 15.79 11.0 92 20.17 11.2 155 17.82 11.2 144 19.04 10.6 38 16.6 11.3 110 16.89 11.1 156 19.59 10.9 66 17.58 10.9	optimized ADRAZB delfins	186	17.42	Ξ	128	18.8	10.5	53	21.95	11.7	1.96	0.14	012 012
131 18.77 10.5 113 15.79 11.0 92 20.17 11.2 155 17.82 11.2 144 19.04 10.6 38 16.6 11.3 110 16.89 11.1 156 19.59 10.9 66 17.58 10.9	urd Optimized ADRAZC ^e dinucleotide repeat Ind	155	18.14	11.5	158	18.46	10.6	23	19.73	9.6	0.215	0.81	102
155 17.82 11.2 144 19.04 10.6 38 16.6 11.3 110 16.89 11.1 156 19.59 10.9 66 17.58 10.9	and Optimized Optimized NET (SLC642) SNP A1970G Man	131	18.77	10.5	5	15.79	11.0	85	20.17	11.2	4.45	0.012	202 102
110 16.89 11.1 156 19.59 10.9 66 17.58 10.9 75 19.42 10.8 10.5 10.5 10.5 10.5 10.5 10.5 10.5 10.5	Optimized PNMT SNP G-148A	155	17.82	11.2	144	19.04	10.6	38	16.6	11.3	0.914	0.402	120 120
75 19.42 10.8 12.5 19.50	Optimized COMT SNP val 158 met, G1947A, Natil	110	16.89	11.1	156	19.59	10.9	99	17.58	10.9	2.05	0 129	012 021
801 16.52 10.0 80 16.52 10.8	Optimized	75	19.42	10.8	175	18.52	11.0	98	16.52	10.8	1.55	0.212	210

Ut, references for literature-based gene scoring; Ind. gene scoring based on our studies of an independent set of subjects; SNP, single nucleotide polymorphism.

1 DRD4; 11 = any <4; 12 = 4/4; 22 = any > 4,

2 DRD5; 11 = 148/148; 12 = hel; 22 = non 148/non 148.

3 DA77; 11 = non 10/non 16; 12 = 10/non 10; 22 = 10/10.

4 HTF: 11 = SS; 12 = SL; 22 = LL.

5 HTR104, TD02 since there were only 2 22s, they were combined with the 12s.

6 ADRA2C: 11 = < 183/ < 183; 12 = hel; 22 = 183/183.

David E. COMINGS METHOD OF PROFILING GENES AS RISK FACTORS FOR ATTENTION DEFICIT Serial No New Attorney Dkt No 1954-332 Sheet 3 of 10

ANOVA of ADHD score for the Genotypes of Twenty Genes

Gene	11			12				22			F-ratio	p	Gene
	% Mean	S.D.	%	Mean	S.	D.	%	Mean	S	.D.			Score
Other Neu	ırotransmitt	ter Genes	<u>s</u>										
HTR6 SN	P (Shinkai	et al. 199	98)										
ADHD	2.8 12.3	3 9.7	27.1	18.20	5	10.3	70.0	18.6	66	11.2	1.44	.23	012
ODD	3.0	2.3		3.9	1	3.1		3.6	54	3.2	.44	.64	021
CD	2.1	1 1.5		3.6	5	2.6		3.3	17	2.6	2.05	.13	022
GABRB3	dinucleoti	ide repea	t (Mu	utirangu	ra e	et al. 1	1992)	a					
ADHD	38.0 18.9	9 10.8	3 47.	9 17.4	8	11.1	14.	1 19.	59	10.9	1.05	.35	102
ODD	3.57	3.1	l	3.5	5	3.2		4.	47	3.1	1.67	.18	002
CD	3.01	2.2	2	2.9	7	2.4		2	.91	2.4	.089	.91	200
					,								
GABBR1	dinucleotic	de repeat	(unp	ublished	d) ^b)							
ADHD	9.5 17.5	5 11.	7 2'	7.0 19	.1	11.7	63.	5 18.	2	10.5	.28	.752	020
ODD	3.5	3.	7	3	.66	3.1		3.	72	3.1		.953	012
CD	3.4	15 2.	6	2	.72	2.2		3.	02	2.4	1.24	.291	201
CNR1 (C	annabinoid	l 1 recept	tor) (l	Dawson	19	95) ^c							
ADHD	10.6 19.35	5 10.	9 4	4.7 18.2	25	11.0	44	.7 18	13	10.9	.174	.83	200
ODD	4.67	7 3.	1	3.5	54	3.1		3	.56	3.2	1.89	.15	200
CD	3.09	9 2.	2	2.9	90	2.3		3	.03	2.4	.140	86. 6	202
										تہ			
CHRNA-	(Choliner	gic, nico	tinic,	alpha 4	7) (Weilaı	nd,St	einlein	199	6) ^a			
ADHD	8.0 22.		36.			10.8	55			11.2	2.35	.096	210
ODD	5.	07 3.0)	3.5	59	3.0		3	.55	3.2	2.74	.065	200
CD	3.	11 2.1	-	2.9	93	2.3		2	.99	2.4	.071	.930	200

David E. COMINGS METHOD OF PROFILING GENES AS RISK FACTORS FOR ATTENTION DEFICIT Serial No New Attorney Dkt No 1954-332 Sheet 4 of 10

NMDAR1	(Rupp et al. 1	997) <i>Hpa</i> II	SNP							
ADHD	44.2 17.31	10.7 45.7	19.31	11.0	10.1	18.56	11.3	1.19	.303	021
ODD	3.79*	3.1	3.79*	3.1		4.84	3.1	2.93	.054	002
CD	2.83	2.3	3.07	2.3		3.28	2.7	.649	.523	012
ADORA2	4 (adenosine	2A receptor)	(Decke	rt et al	. 1996)	C 108 T	Rsa I.			
ADHD	33.2 19.95	10.4 44.7	17.57	11.0	22.0	18.97	10.8	1.48	.229	201
ODD	4.04	3.3	3.41	3.1		4.02	3.1	1.52	.219	202
CD	3.39	2.5	2.82	2.1		2.83	2.4	2.04	.131	200
GRIN2B (glutamate ion	otropic, NM	DA 2B	recepto	or) T/G	(SNP da	atabase	WIAF-	1189).	
ADHD	20.9 17.94	10.6 52.3	19.35	10.6	26.8	18.10	11.1	.582	.559	021
ODD	3.03*	3.0	4.15	3.1		3.50	3.1	3.22	.041	021
CD	2.36*	2.0	3.28	2.4		2.98	2.3	3.59	.029	021
NOS3 (nit	ric oxide syntl	hase 3) (War	ng et al.	1996)						
ADHD	67.5 18.50	10.9 25.0	18.60	10.6	7.5 1	7.12	11.6	.186	.830	220
ODD	3.72	3.1	3.87	3.3		3.29	3.1	.311	.733	120
CD	3.00	2.3	3.12	2.2		2.33	1.9	1.08	.339	120
Opoids										
PENK (pr	oenkephalin)	(Weber,May	1990; (Coming	gs et al.	1999a) ⁶	2			
ADHD	32.1 18.71	10.4 47.4	18.02	11.3	20.6	18.25	11.0	.053	.948	201
ODD	3.75	3.2	3.75	3.2		3.48	3.1	.255	.775	220
CD	3.03	2.4	3.00	2.4		2.92	2.2	.041	.959	220

Figure 1(b) (Continued)

David E. COMINGS METHOD OF PROFILING GENES AS RISK FACTORS FOR ATTENTION DEFICIT Senal No New Attorney Dkt No 1954-332 Sheet 5 of 10

			c							
MME (enk	ephalinase) (s	ee Methods)	f.							
ADHD		11.0 50.9		10.9	15.2	19.53	10.9	1.26	.284	202
ODD	3.98	3.25	3.44	3.1		3.95	3.0	1.00	.369	202
CD	3.10	2.4	2.81	2.3		3.32	2.4	1.08	.340	202
ANPEP (a	minopeptidase	e N) (Watt,V	Villard 1	(990) a	nd see I	Methods	, A 257	7 G		
ADHD	27.7 19.25	10.7 51.6	18.37	10.9	20.8	17.60	11.4	.398	.672	210
ODD	3.65	3.1	3.95	3.1		3.30	3.2	.945	.389	120
CD	3.12	2.4	3.05	2.4		2.42	2.0	1.96	.142	210
NATI (N-	acetyl transfer	ase) T 1088	A (Die	tz et al	. 1997;	Coming	s et al.	2000)		
ADHD	5.7 21.50	9.5 34.7	19.00	11.2	59.6	17.86	10.8	1.11	.329	210
ODD	4.94	3.7	3.51	3.2		3.68	3.1	1.58	.207	200
CD	4.11	2.8	3.00	2.3		2.88	2.2	2.26	.106	210
Hormones	s and neurope	otides								
ESR1 (est	rogen 1 recep	tor) dinucle	otide re	peat (de	el Senno	et al. 1	992; C	omings	et al. 19	999).
ADHD	27.3 19.08	12.0 41.2			31.5		10.3	.673	.511	201
ODD	3.82	3.4	3.56	3.0		3.86	3.0	.293	.746	202
CD	3.26	2.6	2.53	* 2.0		3.33	2.5	4.09	.017	202
<i>CYP19</i> (a	romatase cyto	chrome P-45	50) dinu	cleotid	e repeat	t (Polym	eropou	ılos et al	l. 1991t) ^g
ADHD	13.4 16.88				41.4	19.76		2.11	.122	012
ODD	3.50	3.1	3.33	3.0		4.11	3.3	2.16	.116	102
CD	3.07	2.4	2.52	* 2.2		3.37	2.4	4.61	.011	102

Figure 1(b) (Continued)

David E. COMINGS METHOD OF PROFILING GENES AS RISK FACTORS FOR ATTENTION DEFICIT Serial No New Attorney Dkt No 1954-332 Sheet 6 of 10

SHBP (sex	k hormone bin	ding protein) (Xu,Li 199	8)			
ADHD	59.8 18.39	11.2 35.2	18.38 10.4	5.0	17.44 11.4	.057 .944	220
ODD	3.61	3.1	3.76 3.	Į.	3.50 3.1	.108 .897	120
CD	2.85	2.3	3.11 2.3	3	3.06 1.8	.465 .628	021
CRH (cort	icosterioid rel	easing horm	one) (Xmn I	Genome 1	Database)		
ADHD	89.8 18.25	11.1 8.6	18.78 8.8	1.5	25.00 7.9	1.189 .285	012
ODD	3.66	3.2	3.71 2.8		5.60 3.2	.972 .380	012
CD	2.96	2.4	3.10 2.1		3.80 3.3	.370 .691	012
OXTR (ox	ytocin recepto	or) (Liao et a	1. 1996) sile:	nt C->T in	exon 3		
ADHD	47.1 18.48	10.5 44.3	18.0 11.5	8.7 20	0.11 10.7	.431 .650	102
ODD	3.59	3.1	3.65 3.2	4	4.39 2.8	.776 .461	012
CD	2.77	2.3	3.14 2.3	-	3.14 2.4	1.06 .347	022
CCK C	45 T (Ishiguro	et al. 1999)					
ADHD	77.0 18.57	10.8 20.4	17.66 11.			.227 .797	102
ODD	3.83	3.2	3.30 2.	9	3.00 3.0	.909 .404	210
CD	3.04	2.4	2.71 2.	2	3.14 2.3	.555 .574	102
INS (Hob	an,Kelsey 199						
ADHD	58.6 18.04	10.8 36.7				.147 .863	012
ODD	3.68	3.2	3.70 3		3.66 3.6	.0014 .998	120
CD	2.95	2.3	2.98 2	4	3.47 1.6	.334 .716	002
			h				
CD8 (Pol	ymeropoulos						0.04
ADHD	23.2 17.5	11.3 44.3	18.54 10		18.42 10.9	.122 .885	021
ODD	3.31	3.2		.2	3.44 3.0	1.95 .143	021
CD	2.53	2.1	3.27 2	.5	2.92 2.1	2.44 .088	021

Figure 1(b) (Continued)

David E. COMINGS METHOD OF PROFILING GENES AS RISK FACTORS FOR ATTENTION DEFICIT Serial No New Attorney Dkt No 1954-332 Sheet 7 of 10

INFG (Wu, Comings 1998)

ADHD	21.8 18.22	10.9 58.3	18.17	10.9	27.9	18.82	10.8	.109	.896	102
ODD	3.78	2.97	3.69	3.2		3.60	3.2	.068	.934	210
CD	3.11	2.4	3.01	2.4		2.82	2.0	.333	.717	210

PS1 (Scott et al. 1996)

ADHD	36.0 17.78	11.1 48.0	18.56	10.6	15.2	18.19	11.6	.215	.806	021
ODD	3.44	3.3	3.92	3.1		3.57	3.1	.828	.438	021
CD	2.59	2.1	3.18	2.4		3.30	2.5	2.68	.069	012

^{*} Significantly lower than highest value by tukey test at $\alpha = .05$.

a
$$11 = <188/<188$$
, $12 = het$. $22 = =188/=188$

b
$$11 = =10/=10$$
, $12 = het$. $22 = >10/>10$

c
$$11 = <5/<5$$
 $12 = het$. $22 = =5/=5$

d
$$11 = =131/=131$$
 $12 = het$. $22 = >131/>131$

e
$$11 = 178/=178$$
 $12 = \text{het.}$ $22 = >178/>178$

$$f 11 = a-c/a-c$$
 $12 = het$. $22 = d-g/d-g$

g
$$11 = \frac{4}{4}$$
 $12 = \text{het.}$ $22 = \frac{4}{4}$

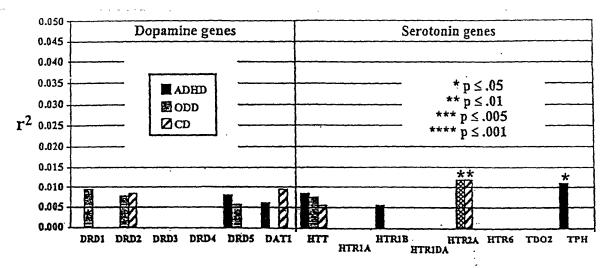
h
$$11 = 145/145$$
 $12 = 145/x$ $22 = x/x$

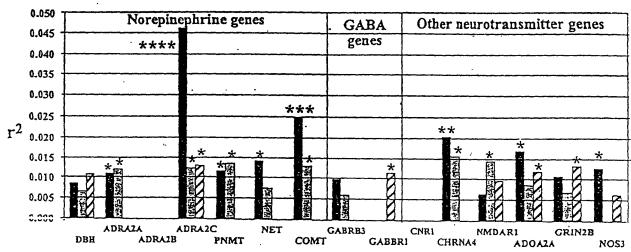
David E. COMINGS METHOD OF PROFILING GENES AS RISK FACTORS FOR ATTENTION DEFICIT Serial No New Attorney Dkt No 1954-332 Sheet 8 of 10

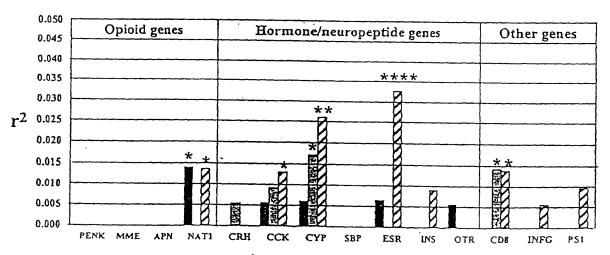
Final Results for the 42 Genes for the ADHD, ODD and CD traits

Trait	r	r^2	adjusted r ²	F	p	# genes
ADHD	.466	.217	.16	3.82	<.0001	22
ODD	.443	.196	.14	3.58	<.0001	20
CD	.451	.203	.15	3.94	<.0001	19

Figure 2







Genes

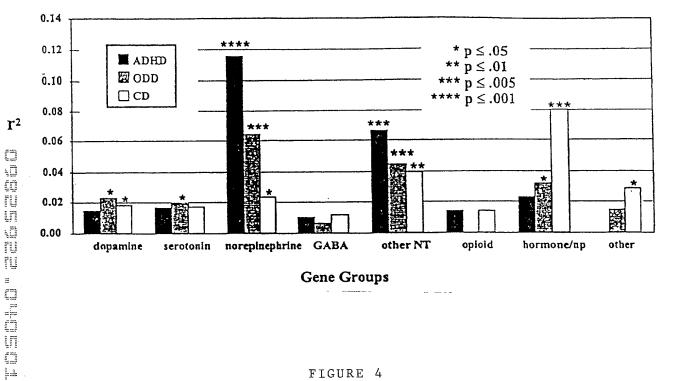


FIGURE 4